REMARKS

Claims 1-102 are currently pending in this application, of which claims 1-7, 9-10, 25-35, 51-52, and 55-56 have been examined. The remaining claims (i.e., claims 8, 11-24, 36-50, 53, 54, and 57-102) have been withdrawn as directed to non-elected subject matter. Claims 1, 10, 25, 35, 52, and 56 have been amended in this response, and claims 8-9, 11-24, 34, 36-50, 53-54, and 57-102 have been cancelled without prejudice or admission.[1] Hence, claims 1-7, 10, 25-33, 35, 51-52, and 55-56 will be pending upon the entry of these amendments. Independent claims 1 and 25 have been amended, without prejudice or admission, to particularly recite the elected subject matter of this invention. In particular, the claims as amended specify methods for identifying cancer cells or tissue (as well as individuals having such cancer cells or tissues) in which the cancer is associated with elevated CAP43 expression. These amendments merely incorporate the limitations of original claims 9 and 34, and therefore are not new matter. Original claims 9 and 34 have therefore been cancelled, without prejudice or admission. Also, dependent claims 10 and 33 (which originally depended from cancelled claims 9 and 34) have been amended so that they now depend from amended claims 1 and 25, respectively. Finally, claims 10, 32, 52, and 56 have been amended to delete the reference to colon cancer and lymphomas and to recite "histiocytoma" instead of "histocytoma." Support for these amendments can be found at Table I, starting on page 75, line 1, page 6, lines 21-23, and Figure 7B. However, the cancellation of the reference to colon cancer and lymphomas is made without prejudice or admission, and Applicants reserve the right to pursue claims for that cancelled subject matter in both this and related (e.g. divisional and continuation) applications.

The specification has been amended in the paragraph starting at page 3, line 23 to correct typographical errors. In particular, the specification has been amended to recite "histiocytoma" instead of "histocytoma." Support for this amendment can be found at Table I, starting on page 75, line 1, page 6, lines 21-23, and Figure 7B. No new matter has been added. This paragraph has also been amended to correct the spelling of "inflammation." The specification has also been amended

[1] Applicants reserve the right to preserve the subject matter of these cancelled claims, as well as any other non-elected subject matter disclosed in this application, both in the instant or in other (e.g., related divisional or continuation) applications.

at page 80, lines 1-8, to correct informalities in the specification. Specifically, the specification has been amended to delete "[??]."

Applicants acknowledge the oral election made to the telephone restriction requirement of January 30, 2004, and acknowledge that the original restriction requirement has been modified accordingly.

As explained above, the amendments presented with this response to not introduce new subject matter to the application. Entry and consideration of the amendments is therefore respectfully requested.

The Objection to the Specification for Lack of Antecedent Basis has been Obviated

The Examiner has objected to the specification for failing to provide antecedent basis for the limitation of "malignant fibrous histocytoma" recited in claims 10, 35, 52, and 56 as originally filed. Applicants note that "malignant fibrous histocytoma" is a typographical error, and that the limitation should in fact read "malignant fibrous histiocytoma." Support for this correction can be found at Table I, starting on page 75, line 1, page 6, lines 21-23, and Figure 7B.

Accordingly, claims 10, 35, 52, and 56 have been amended to recite "malignant fibrous histiocytoma." Antecedent basis for "malignant fibrous histiocytoma" is found at Table I, starting on page 75, line 1, page 6, lines 21-23, and Figure 7B. It is believed that these amendments obviate the Examiner's rejection, and applicants respectfully request that the objection to the specification be withdrawn.

The Objection to Informalities in the Specification has been Obviated

The Examiner has objected to the specification for informalities, specifically, the "see FIGS 11[??]" on page 80, line 8. The specification has been amended to remove the "[??]." This amendment obviates the Examiner's rejection, and applicant's respectfully request that the objection to the specification be withdrawn.

The Rejections Under 35 U.S.C. §112, First Paragraph, Should be Withdrawn:

Claims 1-7, 9-10, 23-35, 51-52, and 55-56 have been rejected under the first paragraph of 35 U.S.C. § 112, for lack of written description. Specifically, the Examiner argues that the specification does not adequately describe CAP43 beyond the particular nucleic acid and protein sequences in SEQ ID NOs: 1 and 2. The Examiner states, citing decisions of the Court of Appeals for the Federal Circuit in *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997), and in *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 296 F.3d 1316, 52 U.S.P.Q.2d 1129 (Fed. Cir. 1999), that to provide adequate written description, Applicants must describe structural features common to a substantial portion of the genus, or, alternatively, disclose "sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Applicants respectfully submit that this rejection should be withdrawn for the reasons set forth below.

Unlike the insulin cDNA molecule at issue in *Eli Lilly*, at the time the application was filed, CAP43 was already well known in the art. Hence, the critical features of CAP43 protein and nucleic acids which the Examiner requests were already well known in the art and need not be specifically enumerated in this application or in the pending claims.[2] Hence the present invention does not claim the CAP43 cDNA or any protein it encodes. Rather, the invention specifies novel methods that invoke detecting the expression of a CAP43 gene or its gene product. Such methods do not require a complete characterization or disclosure of the various homologs and polymorphisms. Rather, it is well recognized in the art that a given gene (e.g., CAP43) can be detected, e.g., using nucleic acids that specifically hybridize to that gene. Simply, a polypeptide such as the CAP43 polypeptide can be readily detected using antibodies that specifically bind to the polypeptide. It is well known by those skilled in the art that such methods can be used to detect homologs and variants of a given gene and its gene products - even where those homologs and variants have not previously been described or characterized. Indeed, these very same methods of detection can also be used to isolate such homologs and variants.

[2] Applicants respectfully direct the Examiner's attention to the disclosures in the specification at page 3, lines 1-20, and the references cited therein.

Additionally, claims 10, 32, 52, and 56 have been rejected under the first paragraph of 35 U.S.C. § 112, for lack of enablement. In particular, the Examiner argues that the application is not enabling for methods of detecting colon cancers, malignant fibrous histocytomas, and lymphomas by detecting increased CAP43 expression, since CAP43 expression in these tissues is decreased or comparable to normal tissue.

Applicant respectfully points out that Claims 10, 32, 52, and 56 have been amended to delete reference to colon cancer and lymphoma. As discussed above, claims 10, 32, 52, and 56 have also been amended to recite "malignant fibrous histiocytoma." The specification provides ample support to show that malignant fibrous histiocytomas demonstrate increased expression of CAP43 relative to normal tissue. See Table I, starting on page 75, line 1, page 6, lines 21-23, and Figure 7B. Thus, a person skilled in the art would be capable of detecting malignant fibrous histiocytomas by the method of the present invention. It is believed that these amendments obviate the Examiner's rejection.

Based upon the foregoing comments, Applicants respectfully submit that the rejections under 35 U.S.C. § 112, first paragraph, should be withdrawn.

The Rejections Under 35 U.S.C. § 101 Should be Withdrawn:

Claims 10, 35, 52, and 56 have been rejected under 35 U.S.C. § 101 for lack of utility. The Examiner bases this rejection upon the same argument used to reject these claims under 35 U.S.C. § 112, first paragraph, as discussed above. The Examiner alleges that since the method of these claims would therefore not work to detect colon cancer, malignant fibrous histocytoma, and lymphoma, the claims therefore lack utility.

As noted above, the independent claims have been amended to more particularly recite preferred embodiments, where the method of this invention are used to diagnose and/or detect cancer associated with elevated levels of CAP43. Claims 10, 35, 52, and 56 have been amended to remove reference to colon cancer and lymphoma, and to recite "malignant fibrous histiocytoma." As discussed above, the specification shows increased staining for CAP43 in malignant fibrous

histiocytomas relative to normal tissue. See Table I, starting on page 75, line 1, page 6, lines 21-23, and Figure 7B. Therefore, based upon the disclosure of the specification, the present invention can be used to detect malignant fibrous histiocytomas based upon increased CAP43 expression. It is believed that these amendments render the Examiner's rejection moot. Therefore, Applicant's respectfully request that the rejection under 35 U.S.C. § 101 be withdrawn.

The Rejections Under 35 U.S.C. § 102(e) Should be Withdrawn:

Claims 1-7, 9, 25-34, 51, and 55 have been rejected under 35 U.S.C. § 102(e) as anticipated in view of U.S. Patent No. 6,376,169 to Adams, et al. ("Adams"). The Examiner alleges that Adams discloses a method of using a gene, referred to in Adams as RTP/DRG/Ndr1, to diagnose diseases that include cancer. The Examiner alleges that the protein sequence of RTP/DRG/Ndr1 is identical to the amino acid sequence set forth in this application for CAP43. Applicants respectfully submit that this rejection should be withdrawn for the reasons set forth below.

Applicants respectfully disagree with the Examiner, and submit that this rejection should be withdrawn. Adams merely teaches that expression of the gene he refers to as RTP/DRG/Ndr1 is increased under hypoxic conditions. See Adams, col. 13, line 57 to col. 14, line 3; col. 22, line 62 to col. 23, line 12; see also col. 2, line 35 to col. 4, line 14 and Figures 1 to 6. Adams demonstrates this in Example 3 (starting at col. 22, line 1) by culturing three-dimensional spheroids of breast tumor cells *in vitro* under normal (20%) oxygen and hypoxic (1% O_2) conditions. Adams reports that RTP/DRG/NDR1 expression is elevated in these cells when grown under hypoxic conditions. However, Adams does not teach that RTP/DRG/Ndr1 is expressed generally by such cells. To the contrary, Adams reports that cells grown under normal conditions do not stain for RTP/DRG/Ndr1 expression. Hence, Adams teaches that RTP/DRG/Ndr1 is only expressed in certain cells when cultured under particular conditions. This does not suggest that RTP/DRG/Ndr1 (i.e., CAP43) can be used to identify cancer cells or to diagnose cancer in an individual. Indeed, since Adams teaches that expression of that gene is <u>not</u> upregulated in cancer cells cultured under normal (i.e., non-hypoxic) conditions, the reference actually teaches away from the presently claimed invention.

Anticipation requires that each and every element of the rejected claim(s) be disclosed in a single prior art reference. M.P.E.P. §2131. See also *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631,. 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Every element of the claimed invention must be literally present, arranged as in the claim. See, *Perkin Elmer Corp.*, 732, F.2d 888, 894, 221 USPQ 669, 673 (Fed. Cir. 1984). As explained above, however, Adams does not describe the detection of cancers not associated with hypoxia. Applicants therefore respectfully submit that the rejection for anticipation should be withdrawn.

The Rejection Under 35 U.S.C. § 102(f)

The Examiner has rejected claims 1-7, 9-10, 25-35, 51-52, and 55-56 under 35 U.S.C. § 102(f) for failing to name the correct inventor of the claimed subject matter. In particular, the Examiner has cited to a thesis Abstract by Hakan Cangul, which, according to the Examiner, appears to describe the claimed invention. The Examiner suggests that Dr. Cangul may have made an inventive contribution to the subject matter claimed in this application, and so rejects the application for not naming him as an inventor. Applicants are currently investigating Dr. Cangul's contributions to the work leading to the invention claimed in this application. Applicants agree that the application will be amended to include the name of Dr. Cangul as a co-inventor if appropriate, i.e., if Dr. Cangul is found to have made a substantial contribution to the complete conception of this invention.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

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Respectfully submitted,

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